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WHAT IS CLAIMED IS

1. An isolated PRE nucleic acid comprising SEQ ID NO:1, the PRE nucleic acid
5 defined as having the following property:
- (i) the PRE nucleic acid, when inserted in a recombinant, hybrid
HIV-1 lacking or having a non-functional wild-type post-transcriptional RNA
nucleo-cytoplasmic transport element (NCTE), is capable of functioning as a NCTE
in the hybrid HIV-1, and when the PRE-containing hybrid HIV-1 virus infects
10 activated human peripheral blood mononuclear cells (huPBMCs), the level of
expression of HIV-1 p24^{gag} is between about 5 fold and about 200 fold less than
levels of p24^{gag} expression when HIV-1 wild type virus, utilizing wild-type NCTE,
infects activated huPBMCs.
- 15 2. An isolated nucleic acid comprising a PRE nucleic acid inserted into a NCTE-
deficient hybrid virus clone, the PRE nucleic acid defined as having the following
properties:
- (i) when an encoded PRE-containing hybrid HIV-1 virus infects
activated human peripheral blood mononuclear cells (huPBMCs), the level of
20 expression of HIV-1 p24^{gag} is between about 5 fold and about 200 fold less than
levels of p24^{gag} expression when HIV-1 wild type virus, utilizing wild-type NCTE,
infects activated huPBMCs; and,
- (ii) the PRE nucleic acid has at least 80% nucleic acid sequence
identity to the sequence set forth in SEQ ID NO:1.
- 25 3. The isolated nucleic acid of claim 2, wherein the PRE nucleic acid is inserted
in place of a wild type nucleo-cytoplasmic transport element (NCTE).
4. The isolated nucleic acid of claim 2, wherein the virus is a retrovirus.
- 30 5. The isolated nucleic acid of claim 4, wherein the retrovirus clone is a HIV
clone.

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6. The isolated nucleic acid of claim 5, wherein the PRE nucleic acid comprises the sequence set forth in SEQ ID NO:1.

5 7. The isolated nucleic acid of claim 6, wherein when the PRE-containing hybrid HIV-1 virus infects activated huPBMCs, the level of expression of HIV-1 p24^{gag} is between about 10 fold and about 50 fold less than levels of p24^{gag} expression when HIV-1 wild type virus infects activated huPBMCs.

10 8. An expression cassette comprising a PRE nucleic acid operably linked to a promoter, wherein the PRE nucleic acid defined as having the following properties:

(i) the PRE nucleic acid, when inserted in a recombinant, hybrid HIV-1 lacking or having a non-functional wild-type post-transcriptional RNA nucleocytoplasmic transport element (NCTE), is capable of functioning as a NCTE in the hybrid HIV-1, and when the PRE-containing hybrid HIV-1 virus infects activated human peripheral blood mononuclear cells (huPBMCs), the level of expression of HIV-1 p24^{gag} is between about 5 fold and about 200 fold less than levels of p24^{gag} expression when HIV-1 wild type virus, utilizing wild-type NCTE, infects activated huPBMCs.; and,

20 (ii) the PRE has at least 80% nucleic acid sequence identity to the sequence as set forth in SEQ ID NO:1.

9. The expression cassette of claim 8, wherein the PRE nucleic acid is SEQ ID NO:1.

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10. The expression cassette of claim 8, wherein the expression cassette is an expression vector.

11. A transfected cell comprising an expression cassette of claim 8.

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12. A recombinant virus, wherein the virus either lacks or has non-functional endogenous post-transcriptional RNA nucleocytoplasmic transport elements

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(NCTEs), further comprising a PRE nucleic acid operatively inserted into the virus, the PRE nucleic acid capable of acting as an exogenous functional NCTE to reconstitute the lacking or non-functional endogenous NCTE and to reconstitute the infectivity of the virus in a mammalian cell,

5 wherein the PRE nucleic acid has at least 80% nucleic acid sequence identity to the sequence as set forth in SEQ ID NO:1.

13. The recombinant virus of claim 12, wherein the virus is a retrovirus.

10 14. The recombinant virus of claim 12, wherein the PRE has at least 90% nucleic acid sequence identity to the sequence as set forth in SEQ ID NO:1.

15. The recombinant virus of claim 14, wherein the PRE comprises a sequence as set forth in SEQ ID NO:1.

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16. The recombinant virus of claim 12, wherein when the PRE-containing hybrid HIV-1 virus infects activated huPBMCs, the level of expression of HIV-1 p24^{gag} is between about 10 fold and about 50 fold less than levels of p24^{gag} expression when HIV-1 wild type virus infects activated huPBMCs.

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17. The recombinant virus of claim 12, wherein the virus is HIV-1.

18. The recombinant virus of claim 12, wherein the insertion of the PRE is in the 3' untranslated region of the virus.

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19. The recombinant virus of claim 17, wherein the insertion of the PRE is in or flanking the Nef region of the HIV-1 virus.

20. The recombinant virus of claim 17, wherein the HIV-1 further lacks a
30 functional Nef.

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21. A vaccine for the prophylaxis or amelioration of a viral infection in a mammal comprising an attenuated retrovirus,
wherein the attenuated retrovirus, when administered as a vaccine in sufficient amounts is capable of eliciting an immune response to the retrovirus in a mammal
- 5 with a functional immune system,
wherein the attenuated retrovirus lacks an endogenous functional post-transcriptional RNA nucleo-cytoplasmic transport element (NCTE) and/or the ability to express an endogenous functional NCTE binding protein, and the attenuated retrovirus further comprises a PRE nucleic acid defined as having the following
- 10 properties:
- (i) the PRE nucleic acid, when inserted in a recombinant, hybrid HIV-1 lacking or having a non-functional wild-type post-transcriptional RNA nucleo-cytoplasmic transport element (NCTE), is capable of functioning as a NCTE in the hybrid HIV-1, and when the PRE-containing hybrid HIV-1 virus infects
- 15 activated human peripheral blood mononuclear cells (huPBMCs), the level of expression of HIV-1 p24^{gag} is between about 5 fold and about 200 fold less than levels of p24^{gag} expression when HIV-1 wild type virus, utilizing wild-type NCTE, infects activated huPBMCs.; and,
- (ii) the PRE has at least 80% nucleic acid sequence identity to the
- 20 sequence as set forth in SEQ ID NO:1.
22. The vaccine of claim 21, wherein the attenuated retrovirus is HIV-1.
23. The vaccine of claim 21, wherein the insertion of the PRE is in the 3' untranslated region of the virus.
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24. The vaccine of claim 22, wherein the insertion of the PRE is in or flanking the Nef region of the HIV-1 virus.
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25. The vaccine of claim 22, wherein the attenuated HIV-1 further lacks a functional Nef.
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26. A kit for the prophylaxis or amelioration of a virus infection in a mammal, the kit comprising a vaccine and a pharmacologically acceptable carrier, wherein the vaccine comprises an attenuated retrovirus,

5 wherein the attenuated retrovirus, when administered as a vaccine in sufficient amounts is capable of eliciting an immune response to the retrovirus in a mammal with a functional immune system,

10 wherein the attenuated retrovirus lacks an endogenous functional post-transcriptional RNA nucleo-cytoplasmic transport element (NCTE) and/or the ability to express an endogenous functional NCTE binding protein, and the attenuated retrovirus further comprises a PRE nucleic acid defined as having the following properties:

15 (i) the PRE nucleic acid, when inserted in a recombinant, hybrid HIV-1 lacking or having a non-functional wild-type post-transcriptional RNA nucleo-cytoplasmic transport element (NCTE), is capable of functioning as a NCTE in the hybrid HIV-1, and when the PRE-containing hybrid HIV-1 virus infects activated human peripheral blood mononuclear cells (huPBMCs), the level of expression of HIV-1 p24^{gag} is between about 5 fold and about 200 fold less than levels of p24^{gag} expression when HIV-1 wild type virus, utilizing wild-type NCTE, infects activated huPBMCs.; and,

20 (ii) the PRE has at least 80% nucleic acid sequence identity to the sequence as set forth in SEQ ID NO:1.

27. The kit of claim 27, further comprising an instructional material teaching the use of the vaccine, wherein the instructional material indicates that the vaccine is used
25 for the prophylaxis or amelioration of HIV-1 infection in a mammal; that the vaccine is to be administered to a mammal in a therapeutically effective amount sufficient to express a viral protein; wherein the vaccine will not cause clinically significant CD4+ cell depletion; and, the expression of the viral protein elicits an immune response to the attenuated HIV-1 virus.

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28. The use of a PRE in the manufacture of a medicament for the prophylaxis or amelioration of a viral infection wherein the PRE is defined as having the following properties:

- (i) the PRE nucleic acid, when inserted in a recombinant, hybrid HIV-1 lacking or having a non-functional wild-type post-transcriptional RNA nucleocytoplasmic transport element (NCTE), is capable of functioning as a NCTE in the hybrid HIV-1, and when the PRE-containing hybrid HIV-1 virus infects activated human peripheral blood mononuclear cells (huPBMCs), the level of expression of HIV-1 p24^{gag} is between about 5 fold and about 200 fold less than levels of p24^{gag} expression when HIV-1 wild type virus, utilizing wild-type NCTE, infects activated huPBMCs.; and,
- (ii) the PRE has at least 80% nucleic acid sequence identity to the sequence as set forth in SEQ ID NO:1.

29. The use of claim 29, wherein the viral infection is an HIV-1 infection.

30. A method for eliciting an immune response to a virus in a mammal, comprising administering to a mammal a therapeutically effective amount of an attenuated recombinant virus, wherein the virus comprises a PRE defined as having the following properties:

- (i) the PRE nucleic acid, when inserted in a recombinant, hybrid HIV-1 lacking or having a non-functional wild-type post-transcriptional RNA nucleocytoplasmic transport element (NCTE), is capable of functioning as a NCTE in the hybrid HIV-1, and when the PRE-containing hybrid HIV-1 virus infects activated human peripheral blood mononuclear cells (huPBMCs), the level of expression of HIV-1 p24^{gag} is between about 5 fold and about 200 fold less than levels of p24^{gag} expression when HIV-1 wild type virus, utilizing wild-type NCTE, infects activated huPBMCs.; and,
- (ii) the PRE has at least 80% nucleic acid sequence identity to the sequence as set forth in SEQ ID NO:1.

31. A method of identifying functional PREs, the method comprising,

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(i) providing a PRE-deficient virus unable to replicate in a cell line;

(ii) ligating nucleic acid fragments into a genome of the virus, thereby constructing a recombinant viral clone;

5 (iii) inserting the recombinant viral clone into the cell line; and

(iv) isolating a nucleic acid comprising a functional PRE from the recombinant viral clone that is propagated in the cell line.